New Ultrasound Signs for Prediction of Early Placental Insufficiency

Original Article

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ABSTRACT

Background: Chronic placental insufficiency is a common condition that affects fetal growth and wellbeing. The response of the fetus to such stress depends on time and degree of placental affection. The acute placental insufficiency rapidly affects the fetal movements, amount of liquor and might lead to fetal demise while the chronic placental insufficiency is more deciduous and affects fetal weight and develops fetal growth restriction more slowly. The prophylaxis against the development of chronic placental insufficiency is more effective to protect growth and avoid perinatal morbidities and moralities.

Aim: Evaluation of 2 new ultrasound signs (tent like placenta and turbid liquor) to predict early placental insufficiency

Materials and Methods: One hundred pregnant women with gestational age between 16 weeks till 28 weeks were included in the study. This cohort of women with singleton pregnancy was evaluated by detailed ultrasound scanning to document gestational age, amniotic fluid index, cerebroplacental ratio (CPR), exclusion of congenital anomalies and other routine ultrasound scanning items. This cohort was divided into two groups, group one was the group with placental tenting and/or turbid liquor while group two was the group with no evidence of placental tenting or turbid liquor.

Results: Documentation of all relevant demographic data was done. The follow up was done every two weeks in all cases unless patients complained of decreased or absent fetal movement, passage of liquor, passage of blood. Spontaneous labour was allowed in primigravidae and elective cesarean section in Cases with previous c-section at completed 38 weeks of gestation was done unless one or more of the following signs had appeared that indicated the need for emergency delivery which were : abnormal low CPR less than 0.76, severe oligohydramnios, biophysical profile equal to or less than 4/8, abnormal cardiotocogram and fetal distress. The duration from the beginning of the study and documentation of the new studied signs in the placenta and turbid liquor till the development of placental insufficiency was calculated in weeks. All complications or adverse events were documented in both groups.

Conclusions: Both new signs were associated with increased risk for development of chronic placental insufficiency and can be used as predictors for evaluation of all pregnant women in the second trimester.

INTRODUCTION

Chronic placental insufficiency is a common serious and potentially dangerous condition with many perinatal morbidity and mortality. Reduction of blood flow may compromise fetuses which have pre-existing hypoxia. The features of reduced baseline variability, decelerations, absence of accelerations suggest hypoxia in the fetus[1].

Since there is a little to be done when diagnosis is made. Many studies tried to predict the development and progression of the placental insufficiency using ultrasound signs notable the uterine artery diastolic notch, fetal weight, doppler study of middle cerebral artery, umbilical artery, and amniotic fluid volume changes[2].

The dilemma of strict definition of fetal growth restriction (FGR) and small for gestational age (SGA) hasn't been solved as there is a considerable overlap between both definitions. Fetal growth restriction (FGR) generally refers to a fetus that has failed to reach its biological growth potential because of placental dysfunction[3].

Among many suggested ultrasonographic signs of decreased placental perfusion is CPR (Cerebroplacental Ratio) that was described for the monitoring of growth-restricted fetuses . It is currently considered as an early sign of placental chronic insufficiency; hence it could discriminate between constitutionally small and growth-restricted fetuses[4].

Many biochemical markers as first trimester (pregnancy-associated placental protein-A and second trimester (total b-hCG and alpha fetoprotein) serum biochemistry could be used.

Screening for placental insufficiency especially in high-risk pregnancies led to many interventions to improve the perfusion hence ameliorate the impact of hypoperfusion on the growing fetus. Many trials to improve the outcome were done using low dose aspirin either from the start of the pregnancy or from week 10 of the gestational age. Anti-thrombolytic therapy was used including low molecular weight heparin with aspirin to prevent recurrence of early pre-eclampsia in patients with inherited thrombophilia[5].

Also, many drugs were tried to improve the placental circulation including sildenafi®l, nitroglycerine®, mini-dose aspirin and antithrombotic therapy[6,7].

Recent advances in novel imaging methods provide the basis for stepwise multi-parametric testing that may deliver cost-effective screening within existing antenatal care systems[8].

AIM OF THE WORK

Evaluation of 2 new ultrasound signs (tent like placenta and turbid liquor) to predict early placental insufficiency

PATIENTS AND METHODS

This study took place in October 2018 till May 2020. This study included one hundred cases of pregnant women came for antenatal care in a private center for high-risk pregnancy. Inclusion criteria: all pregnant women with gestational age between 16 weeks till 28 weeks, age from 18 to 40 years were included in the study. The exclusion criteria included cases with body mass index less than 19 and more than 35 kg/m2 , preterm rupture of membranes or passage of liquor, smokers, chronic medical disease(hypertension, diabetes mellitus and rheumatic diseases) related to risk of low birth weight, positive consanguinity, multiple pregnancy, and known fetal congenital anomalies. This cohort of women with singleton pregnancy were evaluated by detailed ultrasound scanning to document gestational age, amniotic fluid index, cerebroplacental ratio (CPR) and 3 and 4 dimensional USG for exclusion of congenital anomalies. This cohort was divided into two groups, group one was the group with placental tenting and/or turbid liquor while group two was the group with no evidence of placental tenting or turbid liquor.

The placental tenting is the shape of the fetal surface of the placenta projecting into the liquor giving the shape of a tent and this results from the decrease of the pressure of the amniotic fluid needed to keep the fetal side of the placenta stretched. Turbid liquor is cloudiness or haziness of a fluid caused by large numbers of individual particles like smoke in air Figure (1-4).

All women were subjected to detailed medical and obstetric history, routine examination, and ultrasound scanning. Follow up of all cases was done every two weeks unless any complaints emerged. In every visit a
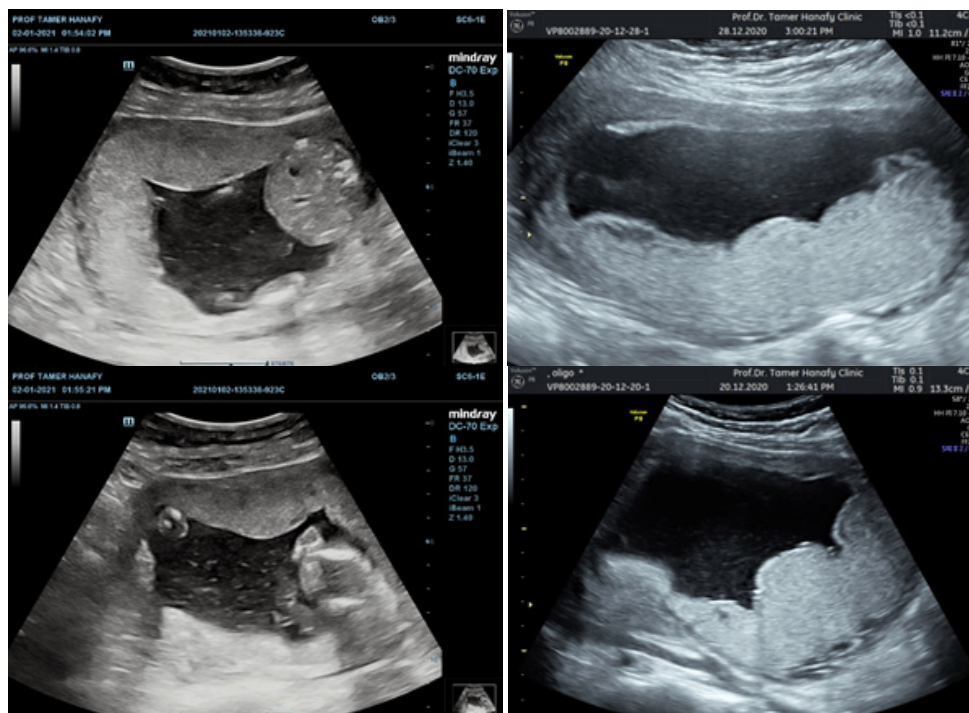

Fig. (1,2,3,4): show both placental tenting and turbid liquor

regular history taking, medical examination and obstetric ultrasound scanning waere done and measurement of AFI, CPR, fetal weight, biophysical profile, and presence of complications were documented[9]. All ultrasound scanning were done by the same sonographer (T.S.) using Voulson P8-version 2 general Electric company.

Documentation of all relevant demographic data was done. The bimonthly follow ups were done in all cases unless patient complained of decreased or absent fetal movement, passage of liquor, passage of blood in any of these previous situations the patient was asked to come and was evaluated immediately and managed accordingly. Spontaneous labour was allowed in primigravidae and elective cesarean section in previous c-section at completed 38 weeks of gestation unless one or more of the following signs appeared that indicated emergency delivery including abnormal low CPR less than 0.76, severe oligohydramnios, biophysical profile equal to or less than 4/8, abnormal cardiotocogram, and fetal distress.

The duration from the documentation of the new sonographic signs (placenta tenting and turbid liquor) till the development of placental insufficiency was calculated in weeks. All complications or adverse events were documented in both groups.

STATISTICAL ANALYSIS

Statistical analysis was performed using the IBM SPSS 20. The Shapiro–Wilk's test was performed to evaluate data distribution of all variables. Age, weight,

parity, uterine size, and procedure time showed a normal distribution, and differences between groups were evaluated by two-tailed Student's t-test for independent data. Differences in pain score between the groups were calculated by T-student test. Statistical significance was set at $P< 0.05$.

RESULTS

This study is a cohort observational one that aimed to evaluate 2 new ultrasound signs that could predict abnormal placental perfusion enough time before its exertion of its unfavorable effects. The demographic and clinical characteristics are demonstrated in (Table 1). The relative risk is 6.6 (95% C. I= 3.1- 14.3). This means that those with placental tenting and or turbid liquor had 6 times risk to develop placental insufficiency. The distribution of the placental signs among both groups are shown in (Table 2).

There is agreement between the presence of placental tenting and or turbid liquor in U/S and the presence of placental insufficiency (kappa statistic = 0.7, *p value* = 0.000) and that 87% of those with placental insufficiency has placental tenting and or turbid liquor compared to 13% of those without tenting or turbid liquor. This difference was statistically significant (chi-square test=46.5, *p value*= 0.000) and the risk estimate is shown in (Table 3). Complications in both groups are demonstrated in (Table 4). The complication rate was statistically significant higher in group (1) than in group (2).

Table 1: Comparison between group one and group two in demographic and clinical characteristics and pregnancy outcome

	Group one Number 50 cases Mean± standard deviation	Group two Number 50 cases Mean± standard deviation	*P value*
Age (years)	29.6 ±5.5	30.8 ±5.8	0.30
Parity (median)	0	1	0.25
Body Mass Index (kg/m2)	26.7±4.3	27.1±4.5	0.63
Gestational age at recruitment (weeks)	23.7±2.5	24.2±2.6	0.28
Amniotic fluid index at recruitment	9.3±2.4	14.4±2.4	0.004*
Amniotic fluid index at delivery	7.1±2	11±1.8	0.005
Cerebroplacental ratio at recruitment	1.1±0.15	1.1±0.14	0.85
Cerebroplacental ratio at delivery	1.2±0.4	1.8±0.3	0.006*
Duration till development of abnormal CPR	9.8±1.6	11.1±0.98	0.06
Complications	34/50 68%	5/50 10%	0.000*

P value is considered significant if less than 0.05

Table 2: Placental tenting sign and or Turbid Liquor * Evidence of abnormal CPR Crosstabulation

| | | Evidence of abnormal CPR | | Total |
		Placental Insufficiency present	Placental Insufficiency absent	
	Count	40	10	50
Group (1)	Percentage	80.0%	20.0%	100.0%
	% within Evidence of abnormal CPR	87.0%	18.5%	50.0%
	Count	6	44	50
Group (2)	Percentage	12.0%	88.0%	100.0%
	% within Evidence of abnormal CPR	13.0%	81.5%	50.0%
	Count	46	54	100
	Percentage	46.0%	54.0%	100.0%

Table 3: Risk Estimate

| | Value | 95% Confidence Interval | |
		Lower	Upper
Odds Ratio for Placental tenting sign and or Turbid Liquor	29.333	9.774	88.031
For cohort Evidence of abnormal CPR = Placental insufficiency present	6.667	3.108	14.302
For cohort Evidence of abnormal CPR = Placental Insufficiency absent	0.227	0.129	0.399
N of Valid Cases	100		

Table 4: Types and number of complications in both groups

	Type of complication	Group (1) Number 50 cases	Group (2) Number 50 cases
	Fetal Growth Restriction	30	3
Complications	Intrauterine fetal death	1	0
	Severe Oligohydramnios	1	0
	Preterm delivery	2	2
No Complications		16 (32%)	45 (90%)

DISCUSSION

Placental insufficiency is a common finding that might lead to perinatal complications and morbidity. Once diagnosis of placental insufficiency is made limited choices are available to prevent the perinatal morbidity and the diagnosis is usually late. The aim of this study arises from the observation that many cases with borderline amniotic fluid index (intermediate oligohydramnios), that considered lower limit of normal, developed placental insufficiency few weeks later after that observation. This study aimed at evaluation of these ultrasound signs to predict early placental insufficiency and to save more time for early interference with supportive measures and improve perinatal outcome and hence decrease complications[10].

Our study showed increased odds of development of early placental insufficiency if any of the two signs present. The presence of fetal hypoxia could increase incidence of oligohydramnios, growth restriction, antepartum fetal distress and stillbirth. Intrapartum complications are fetal hypoxia, acidosis, and higher rate of caesarean delivery. Neonatal complications include hypoglycemia, hyperbilirubinemia, meconium aspiration, persistent fetal circulation, hypoxic-ischemic encephalopathy, hypocalcemia, hyper-viscosity syndrome and necrotizing enterocolitis. Doppler assessment of the uterine, umbilical, middle cerebral vessels are used to identify placental insufficiency[11].

Disruptions in early placental development, together with progressive pathological processes such as thrombosis, necrosis, and oxidative stress, combine to result into clinical syndromes that as a group are often termed 'placental insufficiency'. Pregnancies with these malfunctioned placentae usually complicated by severe pre-eclampsia, 'early onset' intrauterine growth restriction (IUGR), delivery of a small-for-gestational age infant before 34 weeks. Placental insufficiency usually diagnosed late and the prognosis from the time of diagnosis till delivery is not enough to reverse all the consequences resulted from damaged placenta[12]. In our study we observed about 8-11 weeks lapsed between diagnosis of any of proposed signs of prediction of early placental insufficiency and actual

presence of placental insufficiency and this gave us a long time for interference and treatment.

It was suggested that careful evaluation of serum markers offers great promise as a screening tool to identify pregnancies at risk of serious placental insufficiency[13,14] . Many forms of severe placental insufficiency are described and characterized by small placentas with eccentric cords, termed 'chorionic regression', and a reduced maternal blood supply, termed decidual vasculopathy[15]. The placental pathology such as intervillous thrombosis (IVT) may be identified using real-time ultrasound and are termed echogenic cystic lesions[16].

Many ultrasonographic measurements for diagnosis and evaluation of the placental perfusion function and to help in diagnosis of early placental insufficiency have been proposed include uterine artery resistance indices, AFI, umbilical and middle cerebral artery Doppler and CPR. The CPR is considered one of the important tools to diagnose and predict early onset chronic placental insufficiency. We used CPR between 1.0–1.1 as a reference curve[17]. or as a gold standard for diagnosis of impaired placental perfusion and we used CPR cut off at 0.6765 MoM for interference and termination of pregnancy[18,19].

Both AFI and single deepest pocket techniques for identifying true abnormal AF volumes. Both techniques were unreliable for identifying true AF volumes[20]. The signs described in this study are new, simple, and strongly correlated to increased risk for development of early placental insufficiency. This early prediction will give more time to investigate and interfere to prevent abnormal functioning placentae from causing perinatal morbidity and mortality. The increased rate of complications in group (one) was expected and anticipated and early interference prevented neonatal mortality except in one case. These results could be one of the simple answer for the need stated before about the deficiency of a solid screening or prediction tool for early placental insufficiency[21].

Limitation of this study included limited number of patients, lack of neonatology reports of many patients as they delivered in different hospitals, and lack of laboratory results of few patients of inherited thrombophilia and rheumatic diseases.

CONCLUSION

Both new signs were associated with increased risk for development of chronic placental insufficiency and can be used as predictors of placental hypoperfusion and for evaluation of all pregnant women in the second trimester.

RECOMMENDATION

We recommend larger study and early work up to predict and diagnose the real onset and cause of development of early onset chronic placental insufficiency.

Consent for publication: Consent was obtained from all patients regarding participation and publication of the study results with all respect to confidentiality. All authors accept the publication.

CONFLICT OF INTERESTS

There are no conflict of interests.

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